

1   **Title:** Should Corvis Biomechanical Index (CBI) include corneal thickness parameters?

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6    **Running head**

7    aCBI vs CBI

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1 We read with great interest the article by Steinberg et al regarding a modified Corvis Biomechanical  
2 Index (named aCBI in the article) with the elimination of corneal thickness data, including the  
3 Ambrósio's Relational Thickness to the horizontal profile (ARTh).<sup>1</sup>

4 The aim of this study was to provide a proof of concept whether corneal deformation (biomechanics)  
5 alone would be sufficient to separate normal subjects from keratoconus (kc) patients.<sup>1</sup> This was  
6 accomplished by creating the aCBI algorithm without ARTh in a pairwise matching normal and  
7 keratoconic eyes with regards to their central corneal thickness (CCT) and corrected IOP (Dresden  
8 correction). They further compared the accuracy of the new aCBI and the one obtained with the  
9 current CBI that includes ARTh.<sup>2,3</sup>

10 The authors found that in the training sample, the aCBI was more sensitive and more specific than  
11 the CBI, having a higher area under the ROC (Receiver Operating Characteristic) curve (AUC 0.986  
12 x 0.961). However, the current study had a relatively small sample size and lacked from a validation  
13 population to test the algorithm, which are important limitation factors. Furthermore, as the authors  
14 correctly stated, the design of the study does not give the possibility to judge whether the aCBI would  
15 be better in clinical practice as all the patients were matched in thickness, which, by definition,  
16 eliminates the need to have thickness inside the algorithm. Furthermore, the patients were also  
17 matched in Corvis IOP (Dresdner correction) that should be more correlated with age and  
18 biomechanics compared to bIOP<sup>4,5</sup> and might cause a bias. When we designed CBI, we tried many  
19 combinations of parameters, with and without ARTh, and the published outcomes were always better  
20 when including thickness data.<sup>2,3</sup>

21 We agree with the authors that it is an important finding to demonstrate that corneal deformation or  
22 biomechanical response alone is able to differentiate normal from kc patients, but we would like to  
23 demonstrate that CBI is able to separate more efficiently kc patients compared to aCBI when  
24 considering a larger dataset.

1 The aim of this correspondence is to demonstrate the results of applying the aCBI<sup>1</sup> to the two large  
2 datasets used in the CBI original study,<sup>2</sup> and to compare its performance to the published and  
3 validated CBI.

4 We employed the same published population of 658 patients from two clinics: 329 patients (227  
5 healthy and 102 keratoconic) were included from Rio de Janeiro Corneal Tomography and  
6 Biomechanics Study Group, Rio de Janeiro, Brazil (Database 1) and 329 patients (251 healthy and  
7 78 keratoconic) from the Vincieye Clinic in Milan, Italy (Database 2). Dataset 1 was used as training  
8 dataset. Subsequently, aCBI and CBI were validated using Database 2. Statistical analysis was clearly  
9 described in our paper.<sup>2</sup>

10 The ROC curve investigation of the training Dataset 1 displayed an Area Under the Curve (AUC) of  
11 0.964 for aCBI and of 0.977 for CBI (Figure 1A). Similarly, in the validation Dataset 2, the AUC was  
12 0.969 for aCBI and 0.998 for CBI with the same cut-off points (Figure 1B). With the cut off of 0.5 of  
13 aCBI in Dataset 1 the sensitivity was 90.2% and specificity 92.1%; conversely in validation dataset  
14 (2) they were respectively 92.1 and 88%. Sensitivity and Specificity of CBI, as we previously  
15 published<sup>2</sup> were in Dataset 1 94.1% sensitivity and 100% specificity. Similarly, in dataset 2 the same  
16 cut-off point provided 100% sensitivity and 98.4% specificity.

17 There was a significant difference between the ROC curves ( $p=0.0141$ , De Long's test).

18 In conclusion, we commend the authors for demonstrating that this is possible to establish a pure  
19 biomechanical algorithm for distinguishing normal from kc patients. Nevertheless, we still  
20 recommend the use of the validated CBI in clinical practice as it was shown to provide better ROC  
21 curves and, as a consequence, superior sensitivity and specificity compared to aCBI. The superiority  
22 of CBI is explained by the fundamental double role of ARTh as a correction parameter for thickness  
23 and as an independent factor alone for the separation.

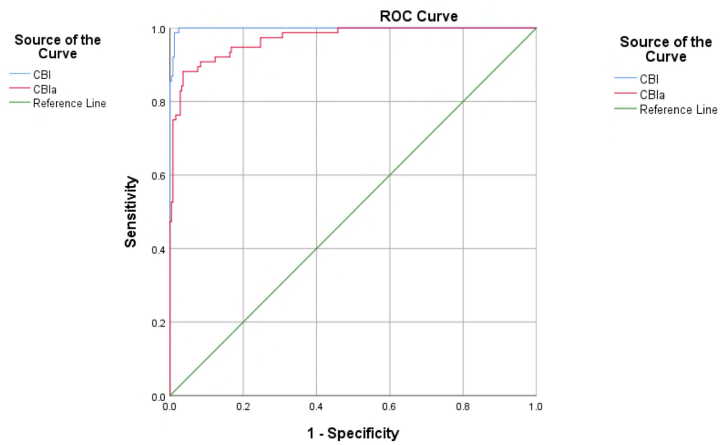
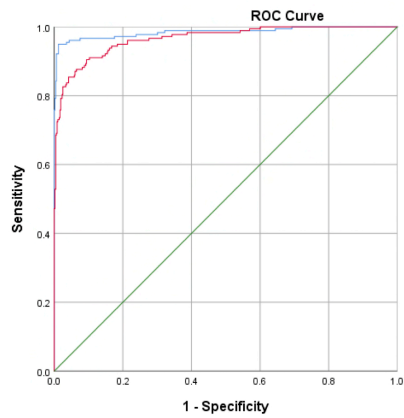


Figure 1 ROC curves of aCBI (blue) and CBI (red) of the training Dataset 1 and validation Dataset 2

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